Appendix K	
Application No. 08/236,402	U.S. Patent No. 5,443,815
Claim 11 (Independent)	
A complex formed by reacting a reagent comprising *the "reagent" can be a peptide since the "specific binding compounds" include peptides -- page 11, lines 13-19*	*Column 4, lines 12-17*: In forming a complex of radioactive technetium with the peptides of this invention, the technetium complex, preferably a salt of Tc-99m pertechnetate, is reacted with the peptides of this invention in the presence of
a specific binding compound having a molecular weight of less than 10,000 daltons,	*Column 3, lines 53-58*: The present invention provides Tc-99m labeled peptides for imaging target sites with a mammalian body that comprise between 4 and 100 amino acid residues and are covalently linked to a radioisotope complexing
the compound being covalently linked to a radiolabel complexing moiety having a formula selected from the group consisting of:	*Column 3, lines 24-38*: . . . covalently linked to radioisotope complexing groups comprising a thiol moiety having the following structure: $A-CH(B)-[C(RR')]_n-X$ wherein A is H or HOOC; B is H, SH or NHR", where R" is H or lower alkyl; X is SH or NHR", where R" is H or lower alkyl; R and R′ are independently H or lower alkyl; n is 0, 1 or 2; and: 1. where B is NHR", where R" is H or lower alkyl, X is SH and n is 1 or 2; and 2. where X is NHR", where R" is H or lower alkyl, B is SH and n is 1 or 2; 4. where B is H, A is HOOC, X is SH and n is 0 or 1; and wherein the thiol moiety is in the reduced form.

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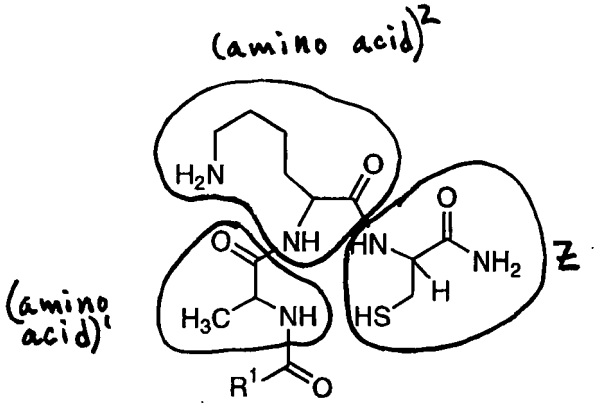
I.

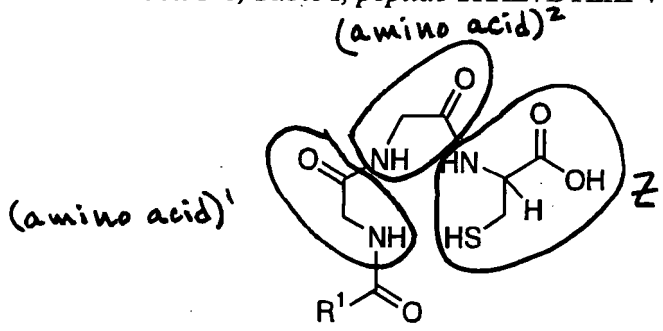
R^1-CO-(amino acid)^1-(amino acid)^2-Z

wherein (amino acid)^1 and (amino acid)^2 are each independently any primary α- or β-amino acid that does not contain a thiol group; Z is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine and 3-mercaptopropylamine; R^1 is lower (C^1-C^4) alkyl or a covalent linkage to the compound;

wherein when Z is cysteine, homocysteine, isocysteine or penicillamine, Z comprises a carbonyl group covalently linked to a hydroxyl group, a NR^3R^4 group wherein R^3 and R^4 are each independently H or lower (C^1-C^4) alkyl, an amino acid, or a peptide comprising 2 to 10 amino acids, and



Col. 5-6, Table I, peptide YRALVDTLKFVTQAEGAKC.NH₂



Col. 5-6, Table I, peptide GRGDGGC

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II.

Y-(amino acid)^2-(amino acid)^1-NHR^2

wherein Y is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoacetate and 3-mercaptopropionate; (amino acid)^1 and (amino acid)^2 are each independently any primary α- or β-amino acid that does not contain a thiol group;

R^2 is selected from the group consisting of H, a lower (C^1-C^4) alkyl, and a covalent linkage to the compound;

wherein when Y is cysteine, homocysteine, isocysteine or penicillamine, Y comprises an amino group covalently linked to -H, an amino acid, or a peptide comprising 2 to 10 amino acids; and

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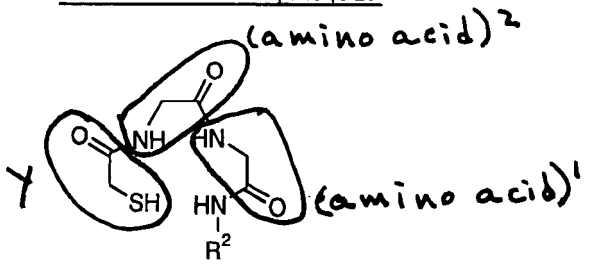
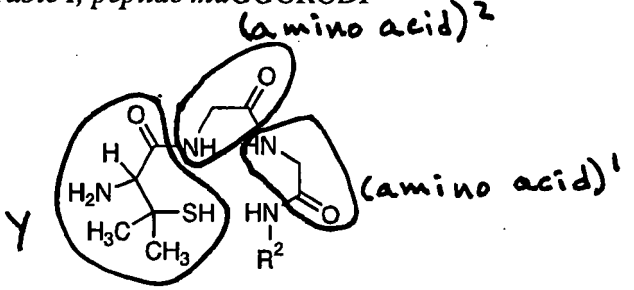
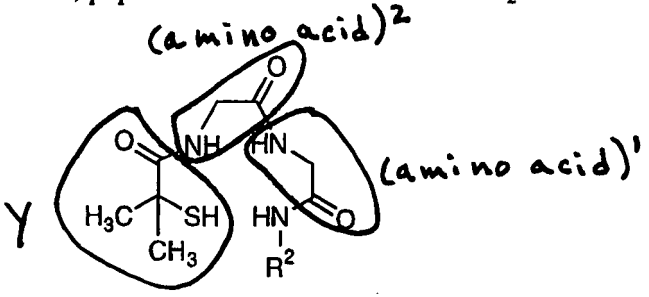


Col. 5-6, Table I, peptide maGGGRGDF



Col. 5-6, Table I, peptide PenGGGRALVDTLK.NH$_2$



Col. 7-8, Table I, peptide mmpGGGRALVDTLK.NH$_2$

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Claim 11 (Independent	
wherein the moiety is linked to the compound through R^1, R^2, a sidechain group of (amino acid)^1, a sidechain group of (amino acid)^2, an amino group of cysteine, homocysteine, isocysteine, or penicillamine, or a carboxyl group of cysteine, homocysteine, isocysteine or penicillamine.	*Column 3, lines 53-58*: The present invention provides Tc-99m labeled peptides for imaging target sites with a mammalian body that comprise between 4 and 100 amino acid residues and are covalently linked to a radioisotope complexing group wherein the complexing group binds a radioisotope.
with technetium 99m in the presence of a reducing agent.	*Column 4, lines 12-17*: In forming a complex of radioactive technetium with the peptides of this invention, the technetium complex, preferably a salt of Tc-99m pertechnetate, is reacted with the peptides of this invention in the presence of a reducing agent;
Claim 1	
A reagent for preparing a scintigraphic imaging agent, comprising a specific binding compound having a molecular weight of less than 10,000 daltons, the compound being covalently linked to a radiolabel complexing moiety having a formula selected from the group consisting of . . .	*Column 3, lines 17-22*: The present invention provides scintigraphic imaging agents that are radioactively labeled peptides. The peptides of the invention are comprised of between 4 and 100 amino acid residues, covalently linked to a radioisotope complexing group wherein the complexing group binds a radioisotope.
See analysis of Claim 11 (independent) for the rest of claim	

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Claim 2	
The reagent of claim 1 wherein the radiolabel complexing moiety is selected from the group consisting of -(amino acid)^1-(amino acid)^2-(amino thiol), and (mercaptocarboxylic acid)-(amino acid)^1-(amino acid)^2 wherein (amino acid)^1 and (amino acid)^2 are each independently any primary α- or β-amino acid; (amino thiol) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoethylamine, and 3-mercaptopropylamine; and(mercaptocarboxylic acid) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoacetic acid, and 3-mercaptopropionic acid.	*See analysis of claim 11 above*
Claim 3:	
The reagent of Claim 2 wherein the radiolabel complexing moiety is selected from the group consisting of -Gly-Gly-Cys- and -Cys-Gly-Gly-.	SEQ ID NO:2
Claim 5	
A reagent according to Claim 1 wherein the compound is a peptide comprising 4 to 100 amino acids	*Column 3, lines 17-22*: The present invention provides scintigraphic imaging agents that are radioactively-labeled peptides. The peptides of the invention are comprised of between 4 and 100 amino acid residues, covalently linked to a radioisotope complexing group wherein the complexing group binds a radioisotope.

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Claim 7	
A scintigraphic imaging agent comprising the reagent according to Claim 1 wherein the radiolabel binding moiety is bound to a radiolabel.	*Column 3, lines 17-22*: The present invention provides scintigraphic imaging agents that are radioactively-labeled peptides. The peptides of the invention are comprised of between 4 and 100 amino acid residues, covalently linked to a radioisotope complexing group wherein the complexing group binds a radioisotope.
Claim 8	
The reagent of Claim 7 wherein the radiolabel is technetium-99m.	*Column 3, lines 59-62*: Labeling with Tc-99m is an advantage of the present invention because the nuclear and radioactive properties of this isotope make it an ideal scintigraphic imaging agent. This isotope has a single photon energy of 140
Claim 12	
The complex of Claim 11, wherein the reducing agent is selected from the group consisting of a dithionite ion, a stannous ion and a ferrous ion.	*Claim 4*: The method of claim 3, wherein the reducing agent is selected from the group of a dithionite ion, a stannous ion, or a solid-phase reducing agent. *(Claim 4 is an original claim.)*
Claim 13	
A complex formed by labeling the reagent of Claim 1 with technetium-99m by ligand exchange of a prereduced technetium-99m complex.	*Column 4, lines 24-29*: Alternatively, the complex may be formed by reacting the peptides of this invention with a pre-formed labile complex of technetium and another compound known as a transfer ligand. This process is known as ligand, exchange and is well known to those skilled in the art.

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Claim 14	
A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed vial containing a predetermined quantity of the reagent of Claim 1 and a sufficient amount of reducing agent to label the reagent with technetium-99m.	*Column 4, lines 54-55*: In a preferred embodiment of the invention, a kit for preparing technetium-labeled peptides is provided.
Claim 15	
A method for labeling a reagent according to Claim 1 comprising reacting the reagent with technetium-99m in the presence of a reducing agent.	*Column 4, lines 12-17*: In forming a complex of radioactive technetium with the peptides of this invention, the technetium complex, preferably a salt of Tc-99m pertechnetate, is reacted with the peptides of this invention in the presence of a reducing agent;
Claim 16	
The method of Claim 15, wherein the reducing agent is selected from the group consisting of dithionite ion, a stannous ion and a ferrous ion.	*Claim 4*: The method of claim 3, wherein the reducing agent is selected from the group of a dithionite ion, a stannous ion, or a solid-phase reducing agent. *(Claim 4 is an original claim.)*
Claim 17	
A method for imaging a site within a mammalian body comprising administering an effective diagnostic amount of the reagent of Claim 2 and detecting a radioactive signal from the technetium-99 localized at the site.	*Column 5, lines 13-21*: Technetium-labeled peptides provided by the as the kidney for diagnosing disorders in these organs, and tumors, such noma and other APUDoma, endocrine tumors such as medullary thyroid ingiomas and astrocytomas, and tumors of the prostate, breast, colon, *Column 5, lines 38-43*: In most instances, a sufficient amount of the administered dose will accumulate in the area to be imaged within about 0.1 of an hour to permit the taking of scintiphotos. Any conventional method of scintigraphic imaging for diagnostic purposes can be utilized in accordance with this invention.